Package: ioncopy (via r-universe)

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Type Package

Title Calling Copy Number Alterations in Amplicon Sequencing Data

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Imports shiny, zip

Description Method for the calculation of copy numbers and calling of copy number alterations. The algorithm uses coverage data from amplicon sequencing of a sample cohort as input. The method includes significance assessment, correction for multiple testing and does not depend on normal DNA controls. Budczies (2016 Mar 15) <doi:10.18632/oncotarget.7451>.

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Contents

`ioncopy-package` *Calling copy number alterations in amplicon sequencing data*

Description

Method for the calculation of copy numbers and calling of copy number alterations. The algorithm uses coverage data from amplicon sequencing of a sample cohort as input. The method includes significance assessment, correction for multiple testing and does not depend on normal DNA controls.

Details

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Author(s)

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References

Jan Budczies, Nicole Pfarr, Albrecht Stenzinger, Denise Treue, Volker Endris, Fakher Ismaeel, Nikola Bangemann, Jens-Uwe Blohmer, Manfred Dietel, Sibylle Loibl, Wilko Weichert, Carsten Denkert: *Ioncopy: a novel method for calling copy number alterations in amplicon sequencing data including significance assessment.* Oncotarget 7(11):13236-47, 2016, doi: 10.18632/oncotarget.7451.

Jan Budczies, Nicole Pfarr, Eva Romanovsky, Volker Endris, Albrecht Stenzinger, and Carsten Denkert: *Ioncopy: an R Shiny app to call copy number alterations in targeted NGS data.* Submitted.

assess.CNA *Significance assessment of copy number alterations*

Description

Starting from a matrix of coverages, the corresponding matrix of copy numbers is calculated. A null model for significance assessment of copy number alterations is fitted. Each amplicon in each sample is assessed for significance. Summarized copy numbers and p-values for genes are calculated as descibed below.

Usage

```
assess.CNA(coverage.target, coverage.source=NULL, method.pooled="amplicon", thres.cov=100)
```

Arguments

coverage.target	A numeric matrix containing the target coverages of each amplicon (rows) in each sample (columns). The target data are investigated for copy number alterations.
coverage.source	A numeric matrix containing the source coverages of each amplicon (rows) in each sample (columns). The source data are used to fit a null model. If NULL, the target data are used to fit the null model.
method.pooled	Method used for the estimation of the null model. Either one common null model for all amplicons (pooled) or individual null models for each of the amplicons (amplicon) are fitted.
thres.cov	Theshold for the minimal mean coverage of an amplicon to be included in the analysis.

Value

List containing the following elements: Matrix of copy numbers with the estimated null model ("model"), estimates of copy numbers ("CN.a" and "CN.g") for amplicons and genes as well as p-values of copy number alterations ("P.a" and "P.g") for amplicons and genes. Copy numbers for genes are calculated as average of the copy numbers of all amplicons interrogating the gene, p-values for genes are calculated using Fisher's method.

Examples

```
## Not run:
data(coverage)
CNA <- assess.CNA(coverage)

## End(Not run)
```

calculate.CN *Calculation of copy numbers*

Description

Starting from a matrix of coverages, the corresponding matrix of copy numbers is calculated. The caluculation includes a sample normalization step and a amplicon normalization step.

Usage

```
calculate.CN(coverage, scale.amplicon=NULL)
```

Arguments

coverage	A numeric matrix containing the coverages of each amplicon (rows) in each sample (columns).
scale.amplicon	Method for amplicon normalization. If NULL the scaling factors are estimated from coverage.

Value

Matrix of copy numbers with the amplicon scaling factors ("scale.amplicon") as attribute.

Examples

```
## Not run:
data(coverage)
CN <- calculate.CN(coverage)

## End(Not run)
```

call.CNA *Gene-wise or amplicon-wise calling of copy number alterations*

Description

Copy number alteration calling after (possible) multiple testing correction for samples and/or amplicons/genes. P-values are controlled either for the number of samples, the number of amplicons/genes or both. Different methods of multiple testing can be chosen to control either FWER or FDR.

Usage

```
call.CNA(CNA, analysis.mode="gene-wise", method.p="samples_genes/amplicons",
method.mt="bonferroni", thres.p=0.05, sig.call=0, sig.per=0)
```

Arguments

CNA	List of CNA assessments generated by assess.CNA.
analysis.mode	The Mode of the analysis: ("gene-wise") or ("amplicon-wise")
method.p	The multiple testing method used for detection: Usage of uncorrected p-values ("p"), p-values corrected for samples ("p_samples"), p-values corrected for amplicons/genes ("p_genes/amplicons") or p-values corrected for samples and amplicons/genes ("p_samples_genes/amplicons").
method.mt	Method for multiple testing correction: must be equal to bonferroni, holm, hochberg, fdr, BH, BY, hommel or none as described in the package stats.
thres.p	Significance level for calling of copy number alterations.
sig.call	An integer >= 0. Only used if analysis.mode="gene-wise". Required minimum number of amplicons supporting a gene CNA call.
sig.per	An integer >= 0. Only used if analysis.mode="gene-wise". Required minimum percentage of amplicons supporting a gene CNA call.

Value

Table containing the status (GAIN, LOSS or NORMAL) of each amplicon or gene in each sample ("tab"). Matrix of copy number estimates in each sample and each amplicon or gene ("CN"). Indicator matrix of detected gains in each sample and each amplicon or gene ("gain") and the same for losses ("loss").

Examples

```
## Not run:
data(coverage)
CN <- calculate.CN(coverage)
CNA <- assess(CN)
calls <- call.CNA(CNA)

## End(Not run)
```

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coverage *Coverage data of 154 amplicons in 184 breast carcinomas*

Description

A matrix of sequencing coverages from semiconductor sequencing

Usage

```
data(coverage)
```

Format

Matrix containing the sequencing coverages of 154 samples (breast carcinomas) and 184 variables (amplicons).

Examples

```
data(coverage)
```

`heatmap.CNA` *Visualization of Copy Number and CNA Calls*

Description

Heatmap visualization including optional hierarchical clustering of amplicons/genes and samples.

Usage

```
heatmap.CNA(CNA, thres.percent=1, cluster.genes=TRUE, cluster.samples=TRUE,
type="CNA calls", method.dist="manhattan", method.link="average", mar=3, cex=0.50)
```

Arguments

`CNA`	Indicator matrix of CNAs generated by `call.CNA`.
`thres.percent`	Number between 0 and 100. Only genes with a minimum percentage of amplified and/or deleted samples are included into the heatmap.
`cluster.genes`	Logical value. If `TRUE` hierarchical cluster of genes is executed.
`cluster.samples`	Logical value. If `TRUE` hierarchical cluster of samples is executed.
`type`	Heatmap of copy numbers `"Copy Number"` or CNA calls `"CNA Calls"`.
`method.dist`	Character. Method for calculation of the distance between genes/amplicons and between samples.
`method.link`	Character. Linkage method to calculate the distance between clusters.
`mar`	Numeric value. Margins for row names and column names.
`cex`	Numerical value. Shrinkage factor for row names and column names.

Value

Depending on `"type"` heatmap of CNAs (color coding: LOSS=green, NORMAL=black, GAIN=red) or heatmap of copy numbers (color coding CN<1: green, CN<2: darkgreen, CN>3: darkred, CN>4: red, CN>5: orange, CN>10: yellow).

read.coverages *Helper function to read coverages from file system*

Description

Coverages are read from tab separated files and stored in a coverage matrix. All coverage files need to refer to the same panel of targets.

Usage

```
read.coverages(chip.names, file.names, anno.col="Target")
```

Arguments

chip.names	A character vector comprizing the chip names.
file.names	A character vector compizing the names of tab separated files. Each file should contain the coverages of the same sequencing panel (rows) in a cohort of samples (columns).
anno.col	The column in input files that compizes the names of the targets. The targets must belong to the same sequencing panel for all input files.

Value

Matrix of coverages of each target sequence (rows) in each sample (colums).

runIoncopy *Shiny app for Ioncopy*

Description

Running Ioncopy as web application.

Usage

```
runIoncopy()
```

summarize.CNA *Summary of CNA calls*

Description

CNA calls are summarized to tables of all amplifications in each sample and to all amplifications in each amplicon/gene.

Usage

```
summarize.CNA(calls)
```

Arguments

calls	List of CNA calls generated by call.CNA.

Value

List of summary matrices for samples ("samples") and amplicons ("amplicon") or genes "gene".

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